

Please replace the "paragraphs" that include the table designation, table title, and the first four (4) SEQ ID NO: entries of Table 19 on page 148, with the following replacement "paragraphs":

Table 19
Factor V Mutations and Genome-Correcting Oligos

Clinical Phenotype & Mutation	Correcting Oligos	SEQ ID NO:
Factor V deficiency Ala221Val GCC-GTC	TTGACTGAATGCTTATTTTGGCCTGTGTCTCTCCCTCTTTCTCA GATATAACAGTTTGTGCCCATGACCACATCAGCTGGCATCTGC TGGGAATGAGCTCGGGGCCAGAATTATTCTCCAT	4340
	ATGGAGAATAATTCTGGCCCCGAGCTCATTCCCAGCAGATGC CAGCTGATGTGGTCATGGGCACAACTGTTATATCTGAGAAAG AGGGAGAGACACAGGCCAAAATAAGCATTCACTCAA	1769
	AGTTTGTGCCCATGACC	1770
	GGTCATGGGCACAACT	1771

IN THE CLAIMS:

Please cancel claims 1 - 24 without prejudice to applicants' prosecuting these claims in one or more continuation or divisional applications.

Please add the following new claims:

25 (new). A method of targeted sequence alteration of a nucleic acid, comprising:

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E1

combining the targeted nucleic acid in the presence of cellular proteins with a single-stranded oligonucleotide 17 - 121 nucleotides in length, said oligonucleotide having an internally unduplexed domain of at least 8 contiguous deoxyribonucleotides,

C8

wherein said oligonucleotide is fully complementary in sequence to the sequence of a first strand of the nucleic acid target, but for one or more mismatches as between the sequences of said oligonucleotide DNA domain and its complement on said target nucleic acid first strand, each of said mismatches positioned at least 8 nucleotides from said oligonucleotide's 5' and 3' termini, and

wherein said oligonucleotide has at least one terminal modification selected from the group consisting of: at least one terminal locked nucleic acid (LNA), at least one terminal 2'-O-Me base analog, and at least three terminal phosphorothioate linkages.

26 (new). The method of claim 25, wherein said sequence alteration is substitution of at least one base.

27 (new). The method of claim 25, wherein said sequence alteration is a deletion of at least one base.

28 (new). The method of claim 25, wherein said alteration is an insertion of at least one base.

29 (new). The method of claim 25, wherein said target nucleic acid is DNA.

30 (new). The method of claim 29, wherein said DNA is double-stranded DNA.

31 (new). The method of claim 30, wherein said double-stranded DNA is genomic DNA.

32 (new). The method of claim 31, wherein said genomic DNA is chromosomal.

33 (new). The method of claim 32, wherein said chromosome is an artificial chromosome.

34 (new). The method of claim 31, wherein said genomic DNA is episomal.

35 (new). The method of claim 25, wherein said cellular proteins are purified.

36 (new). The method of claim 25, wherein said cellular proteins are present in a cell-free protein extract.

37 (new). The method of claim 25, wherein said cellular proteins are present within an intact cell.

38 (new). The method of claim 37, wherein said cell is cultured *ex vivo*.

39 (new). The method of claim 37, wherein said cell is within a living subject.

40 (new). The method of claim 25, wherein said proteins are of a cell selected from the group consisting of: prokaryotic cells and eukaryotic cells.

41 (new). The method of claim 40, wherein said cell is a prokaryotic cell.

42 (new). The method of claim 41, wherein said prokaryotic cell is a bacterial cell.

43 (new). The method of claim 42, wherein said bacterial cell is an *E. coli* cell.

44 (new). The method of claim 40, wherein said cell is a eukaryotic cell.

45 (new). The method of claim 44, wherein said eukaryotic cell is a yeast cell, plant cell, human cell, or a mammalian cell.

46 (new). The method of claim 45, wherein said eukaryotic cell is a yeast cell.

47 (new). The method of claim 46, wherein said yeast is *Saccharomyces cerevisiae*, *Ustilago maydis*, or *Candida albicans*.

48 (new). The method of claim 45, wherein said eukaryotic cell is a plant cell.

49 (new). The method of claim 45, wherein said eukaryotic cell is a human cell.

50 (new). The method of claim 49, wherein said human cell is selected from the group consisting of liver cell, lung cell, colon cell, cervical cell, kidney cell, epithelial cell, cancer cell, stem cell, embryonic stem cell.

Sub E3

51 (new). The method of claim 45, wherein said eukaryotic cell is a mammalian cell.

52 (new). The method of claim 51, wherein said mammal is selected from the group consisting of: mouse hamster, rat, and monkey.

53 (new). The method of claim 25, wherein said oligonucleotide is at least 25 nucleotides in length.

Sub B
Sub G

54 (new). The method of claim 25, wherein said oligonucleotide is no more than 74 nucleotides in length.

55 (new). The method of claim 25, wherein said oligonucleotide is no more than 121 nucleotides in length.

56 (new). The method of claim 25, wherein said first strand is the nontranscribed strand of the target nucleic acid.

Sub E4

57 (new). The method of claim 25, wherein the sequences of said oligonucleotide DNA domain and of the target nucleic acid first strand are mismatched at a single nucleotide.

58 (new). The method of claim 25, wherein the sequences of said oligonucleotide DNA domain and of its

Sub E
complement on the target nucleic acid first strand are mismatched at two or more nucleotides.

59 (new). The method of claim 25, wherein said at least one terminal modification is at least one 3' terminal LNA analogue.

60 (new). The method of claim 59, wherein said oligonucleotide has no more than 3 LNA analogues at its 3' terminus.


61 (new). The method of claim 59, wherein said oligonucleotide has at least one LNA at its 3' terminus and at least one LNA at its 5' terminus.

62 (new). The method of claim 61, wherein said oligonucleotide has no more than 3 contiguous LNA at each of its 3' or 5' termini.

63 (new). The method of claim 25, wherein said at least one terminal modification is at least one 2'-O-methyl ribonucleotide analog at its 3' terminus.

64 (new). The method of claim 63, wherein said oligonucleotide has no more than 4 contiguous 2'-O-methyl ribonucleotide analogs.

65 (new). The method of claim 63, wherein said oligonucleotide has at least one 2'-O-methyl ribonucleotide analog at its 3' terminus and at least one 2'-O-methyl ribonucleotide analog at its 5' terminus.

 66 (new). The method of claim 65, wherein said oligonucleotide has no more than 4 contiguous 2'-O-methyl ribonucleotide analogs.

67 (new). The method of claim 25, wherein said at least one terminal modification comprises at least three terminal phosphorothioate linkages.

68 (new). The method of claim 67, wherein said phosphorothioate linkages at said oligonucleotide's 3' terminus.

69 (new). The method of claim 67, wherein said oligonucleotide comprises no more than 6 contiguous phosphorothioate linkages.

508
Sub
G2

70 (new). The method of claim 25, wherein said targeted nucleic acid is selected from the group of human genes consisting of: ADA, p53, beta-globin, RB, BRCA1, BRCA2, CFTR, CDKN2A, APC, Factor V, Factor VIII, Factor IX, hemoglobin alpha 1, hemoglobin alpha 2, MLH1, MSH2, MSH6, ApoE, LDL receptor, UGT1, APP, PSEN1, and PSEN2.

71 (new). The method of claim 70, wherein said targeted nucleic acid is the human beta-globin gene.

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ES

72 (new). The method of claim 71, wherein said human beta-globin gene is targeted in a human stem cell.

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G2

73 (new). The method of claim 25, wherein said oligonucleotide is 17 - 121 nucleotides in length and includes the sequence of any one of SEQ ID NOs: 1 - 4340.

74 (new). The method of claim 73, wherein said oligonucleotide has sequence identical to any one of SEQ ID NOs: 1 - 4340.

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ES

75 (new). A method of targeted sequence alteration of a nucleic acid, comprising:
combining the targeted nucleic acid in the presence of cellular proteins with a single-stranded oligonucleotide

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17 - 121 nucleotides in length, said oligonucleotide having an internally unduplexed domain of at least 8 contiguous deoxyribonucleotides,

wherein said oligonucleotide is fully complementary in sequence to the sequence of a first strand of the nucleic acid target, but for one or more mismatches as between the sequence of said oligonucleotide DNA domain and the complement thereof on the target nucleic acid first strand, each of said mismatches positioned at least 8 nucleotides from each of said oligonucleotide's termini, and

C8
wherein said oligonucleotide has at least one terminal modification and includes the sequence of any one of SEQ ID NOS: 1 - 4340.

Sub E6
76 (new). The method of claim 75, wherein said at least one terminal modification is selected from the group consisting of: at least one terminal locked nucleic acid (LNA), at least one terminal 2'-O-Me base analog, and at least three terminal phosphorothioate linkages.

77 (new). The method of claim 75, wherein said target is chromosomal genomic DNA.